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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,577	05/26/2005	Andreas Bergmann	2582.009	2150

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EXAMINER	
WEN, SHARON X	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
10/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,577	BERGMANN ET AL.	
	Examiner	Art Unit	
	SHARON WEN	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/26/2009 has been entered.

2. Applicant's amendment, filed 06/22/2009, has been entered.

Claims 1-12 have been canceled.

Claims 13-17 are pending and currently under examination as they read on a method of for the detecting thyroid stimulating hormone (TSH) receptor autoantibodies in a biological sample.

3. This Action will be in response to Applicant's Arguments/Remarks, filed 02/26/2009.

The rejections of record can be found in the previous Office Actions.

Priority

4. In view of Applicant's amendment, filed 01/28/2008, the domestic priority date for claims 13-17 is deemed the effective filing date of PCT/EP03/12129, i.e., 10/31/2003.

Applicant's claim for foreign priority is acknowledge. However, there does not appear to be a certified translation of the priority document, 10255144.8. Therefore, Examiner cannot determine whether the priority document provides sufficient written support for claims currently under examination, i.e., claims 13-17.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 13-17 stand rejected under 35 U.S.C. 102(b) as being anticipated by Parmentier et al. (U.S. Patent 6,228,597 B1, reference of record, see entire document) as evidenced by Weir et al. (*Handbook of Experimental Immunology in Four Volumes*, Volume 1: Immunochemistry, Forth Edition, 1986, Blackwell Scientific Publications, Palo Alto, CA, USA, pages 34.7-34.8, reference of record).

Applicant's arguments, filed 02/26/2009, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant argues that the assay disclosed by Parmentier et al. differs from the claimed method in that the prior art measures the displacement of radio-labeled TSH (125I-TSH) from the receptor by patient's autoantibodies, not, as in the claimed method, the displacement of autoantibodies by autoantibodies. In response, the following is noted: Parmentier et al. clearly taught using labeled autoantibodies to compete for binding of TSH receptor with the autoantibodies in patient's sample (see column 9, lines 12-22 cited below for Applicant's convenience).

> One such assay falling within the terms of the invention is a process for the quantitative detection of thyrotropine (TSH) or of anti-thyrotropine receptor antibodies (anti-TSHr) in a biological sample characterised in that a polypeptide according to the invention is contacted with the biological sample suspected of containing TSH or anti-TSHr antibodies and, either simultaneously or subsequently, contacted with labelled TSH, or **with labelled anti-TSHr antibodies** and the remaining, bound labelled TSH or bound labelled anti-TSHr antibodies after competition between the labelled and unlabelled species, is measured.

Applicant further argues that Parmentier et al. differs from the clamed method in that the prior art autoantibodies were obtained from patient sera by ammonium sulfate

fractionation of the patient sera, not affinity purified against the TSH receptor as claimed. In response to Applicant's argument, following is noted:

The immunoglobulin prepared using ammonium sulfate precipitation from Grave's patient sera was not used as the labeled autoantibodies in the detection assay (see paragraph bridging columns 14-15).

Although Parmentier et al. did not teach that the antibody is obtained by affinity purification, *per se*, given the prior art taught the same or nearly the same method of detecting TSH receptor autoantibodies in a biological sample (see column 9, lines 12-22 cited above and claim 9), and that affinity purification process does not appear to change or add any structural properties to the labeled anti-TSHr antibodies used in the assay; under the broadest reasonable interpretation, the same antibody can also be obtained by affinity chromatography. Therefore, the affinity purified limitation of the labeled autoantibodies is deemed a product-by-process limitation. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Therefore, the rejection of record is **maintained** for the reasons of record, as it applies to the amended and newly added claims. The rejection of record is incorporated by reference herein, as if reiterated in full.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. In view of Applicant's argument and amendment, filed 06/22/2009, the previous rejected under 35 U.S.C. 103(a) as being unpatentable over Parmentier et al. (U.S. Patent 6,228,597 B1) in view of Brown et al. (*J. of Clinical Endocrinology and Metabolism*, 1983, 56:156-163, cited in IDS) has been withdrawn.

New Grounds of rejection are set forth herein.

Claims 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parmentier et al. (U.S. Patent 6,228,597 B1) in view of Morris et al. (Autoimmunity 1994, 17:287-299).

Parmentier et al. taught a method for the detection of TSH receptor autoantibodies in a biological sample comprising contacting said biological sample with TSH receptor that is immobilized on a solid support in the presence of labeled anti-TSH receptor autoantibodies in the biological sample to competitively bind to the TSH receptor and detecting TSH receptor autoantibodies in the biological sample by measuring the amount of label bound to the TSH receptor (e.g., see column 8, lines 59-68; column 9, lines 1-22; column 10, lines, 6-10, 49-55; and claims 9-10).

Although Parmentier et al. did not explicitly teach the labeled anti-TSH receptor autoantibodies were obtained by affinity purification against THS receptor, it would have been obvious to one of ordinary skill in the art, at the time of the invention was made, to perform affinity purification using TSH receptor as the antigen of choice as well as using the affinity-purified anti-TSH receptor autoantibodies as a labeled antibody in the detection assay because affinity purification of anti-TSH receptor autoantibodies from Graves' patient's sera as evidenced by Morris et al. (see entire document). In particular, Morris et al. taught using human TSH receptor extracellular domain peptides as the antigen in the affinity chromatography for the purification of anti-TSH receptor autoantibodies (see e.g., **Introduction** on page 288 and **Affinity Purification of Anti-TSHr Autoantibodies** on page 289). One of ordinary skill in the art would have been motivated to use the extracellular domain peptides of the TSH receptor taught by Morris to affinity purify the anti-TSH-receptor autoantibodies because Parmentier et al. also taught that the extracellular domain of the TSH receptor is ideal to prepare antibodies

that can be used in a variety of studies and assays (see paragraph bridging columns 8-9). Furthermore, one of ordinary skill in the art would have reasonable expectation of success to use the TSH receptor for affinity purification because it is within his/her technical grasp at the time of the invention was made. Moreover, it would also be routine to check the specific activity, as a result-effective variable, of the purified antibodies in a bioassay such as that disclosed by Morris et al. (see Thyroid Stimulating Antibody Bioassay on page 289).

Therefore, the invention, as a whole, was *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claim 13 **stands** rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 6,228,597. Although

the conflicting claims are not identical, they are not patentably distinct from each other for reasons stated in the previous Office Actions, mailed 09/17/2007 and 04/16/2008.

Given the absence of a rebuttal to the outstanding rejection of record, it appears that Applicant has acquiesced to the rejection of record. Therefore the rejection stands for the reasons of record.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Examiner, Art Unit 1644
October 26, 2009